Induction of muscle stem cell quiescence by the secreted niche factor Oncostatin M.

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Public Summary:
Defects in stem cell quiescence, activation, or self-renewal have been implicated in diseases including aging-associated sarcopenia, muscular dystrophy, and cancer cachexia. However, identifying the molecules that control whether or not a cell enters quiescence, activation, or self-renewal has been difficult. Here the authors report a live imaging screen to identify such factors. They identify Oncostatin M as a reversible quiescence inducer.

Scientific Abstract:
The balance between stem cell quiescence and proliferation in skeletal muscle is tightly controlled, but perturbed in a variety of disease states. Despite progress in identifying activators of stem cell proliferation, the niche factor(s) responsible for quiescence induction remain unclear. Here we report an in vivo imaging-based screen which identifies Oncostatin M (OSM), a member of the interleukin-6 family of cytokines, as a potent inducer of muscle stem cell (MuSC, satellite cell) quiescence. OSM is produced by muscle fibers, induces reversible MuSC cell cycle exit, and maintains stem cell regenerative capacity as judged by serial transplantation. Conditional OSM receptor deletion in satellite cells leads to stem cell depletion and impaired regeneration following injury. These results identify Oncostatin M as a secreted niche factor responsible for quiescence induction, and for the first time establish a direct connection between induction of quiescence, stemness, and transplantation potential in solid organ stem cells.